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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/395,677 09/13/99 BERGER

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EXAMINER

FORMAN, B

ART UNIT	PAPER NUMBER
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1655

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DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/395,677	BERGER ET AL.
	Examiner	Art Unit
	BJ Forman	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

#### Status

1) Responsive to communication(s) filed on 13 September 1999.

2a) This action is FINAL.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-32 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-32 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) All b) Some \* c) None of the CERTIFIED copies of the priority documents have been:

1. received.

2. received in Application No. (Series Code / Serial Number) \_\_\_\_\_.

3. received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

#### Attachment(s)

14) Notice of References Cited (PTO-892)                    17) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_

15) Notice of Draftsperson's Patent Drawing Review (PTO-948)                    18) Notice of Informal Patent Application (PTO-152)

16) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                    19) Other: \_\_\_\_\_

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## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-32 are indefinite in the recitation "effective" because it is unclear what the "effect" (function) is (see MPEP 2173.05(c)). It is suggested that the claims be amended to clarify e.g. "a composition comprising a substance having a concentration effective for precipitating or denaturing protein and effective for aiding the infusion....".

Claims 1-32 are indefinite in the recitation "capable of" because it is unclear whether the recitation is a method step i.e. the substance precipitates or a property of the substance i.e. the substance is a precipitating agent. It is suggested that the claims be amended to delete "capable of".

### ***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-9, 13-16, 18, 25-27, 31 & 32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992).

Regarding Claim 1, Bresser et al. disclose a method for stabilizing the structure and nucleic acids of at least one cell in a sample comprising adding to a vessel containing the sample a composition comprising a substance capable of precipitating or denaturing proteins i.e. alcohol (Column 7, lines 39-40) and capable of aiding in the infusion of said composition into said cell i.e. alcohol (Column 2, lines 3-4) or other alcohol and permeation enhancers (Column 5, lines 10-15), contacting said cell in said sample with said composition (Column 10, lines 36-39), incubating said sample with said composition for an effective period of time i.e. 30 minutes and at an effective temperature i.e. 42°C (Column 10, lines 40-42), obtaining said cell with stabilized structure and nucleic acids.

Regarding Claim 2, Bresser et al. disclose the method wherein the substance is an alcohol and/or dimethyl sulfoxide (Column 8, lines 65-67, Column 9, lines 1-17, Column 10, lines 34-39 and Example 4, Column 13-14).

Regarding Claims 3, Bresser et al. disclose the method wherein the substance is methanol (Column 7, lines 39-40).

Regarding Claim 4, Bresser et al. disclose the method wherein the substance is dimethyl sulfoxide (Example 4, Columns 13-14).

Regarding Claims 5-6 Bresser et al. disclose the method wherein the cell is eukaryote, prokaryote or a microorganism (Column 6, lines 14-18).

Regarding Claims 7-9, Bresser et al disclose the method wherein the nucleic acid is DNA, RNA or ribosomal RNA (Column 6, lines 45-48).

Regarding Claim 13, Bresser et al. disclose a method for stabilizing the structure and nucleic acids of at least one cell the method comprising adding to a vessel containing the sample a composition comprising an effective concentration of a substance capable of precipitating proteins i.e. alcohol (Column 7, lines 39-40) and a second substance to aid in the infusion of the first substance into said cell i.e. DMSO (Column 2, lines 50-55, and Claim 1),

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contacting said cell in said sample with said composition, incubating said sample with said composition for a period of time i.e. 30 minutes at a temperature i.e. 42 °C (Column 10, lines 40-42), to obtain at least one cell with stabilized structure and nucleic acids (Example 4).

Regarding Claim 14, Bresser et al disclose the method wherein the alcohol is selected from the group consisting of methanol, ethanol (Column 7, lines 39-40), propanol, isopropanol, butanol (Column 5, lines 46-47).

Regarding Claim 15, Bresser et al. disclose the method wherein the second substance is selected from the group consisting of dimethyl sulfoxide, ethylene glycol and polyethylene glycol (Column 5, lines 13-15).

Regarding Claim 16, Bresser et al disclose the method wherein the first substance is comprised of one alcohol (Column 2, lines 50-54 and Claim 1, lines 26).

Regarding Claim 18, Bresser et al. disclose the method wherein the first substance is comprised of a first alcohol i.e. polyethylene glycol and a second alcohol i.e. dithiothreitol (Hybridization Cocktail, Column 8, lines 65-67 and Column 9, lines 1-4).

Regarding Claims 25-27, Bresser et al disclose the method wherein the nucleic acid is DNA, RNA or ribosomal RNA (Column 6, lines 45-48).

Regarding Claims 31-32, Bresser et al. disclose the method wherein the cell is eukaryote, prokaryote or a microorganism (Column 6, lines 14-18).

#### ***Claim Rejections - 35 USC § 102/103***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 17 & 20 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992) as applied to Claim 16 above. Bresser et al. teach the method wherein the composition comprises a first substance comprised of an alcohol (Column 2, lines 50-54 and Claim 2). Bresser et al. do not teach the ratio of said first and said second substance is 4:1 or 1:1. However, Bresser et al. teach the composition wherein said first substance i.e. alcohol is 2-20 percent of the composition and wherein said second substance i.e. dimethyl sulfoxide 2-20 percent of the composition (Column 2, lines 50-54 and Claim 2). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made that the ratios recited in Claims 17 & 20 i.e. 4:1 and 1:1 would be inherent in the 2 to 20% recited in Bresser et al. and it would have been further obvious to the skilled practitioner apply the range of percentages taught by Bresser et al. to optimize precipitation and infusion based on cell type being assayed and desired results.

6. Claim 19 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992) as applied to Claim 18 above. Bresser et al. disclose the method wherein the first substance is comprised of a first alcohol i.e. polyethylene glycol and a second alcohol i.e. dithiothreitol (Hybridization Cocktail, Column 8, lines 65-67 and Column 9, lines 1-4). Bresser et al. do not teach the method wherein the concentrations of said first and second

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substances are in a ratio of 2.5: 2.5: 5. However, Bresser et al. teach the composition wherein said first substance i.e. alcohol is 2-20 percent of the composition and wherein said second substance i.e. dimethyl sulfoxide 2-20 percent of the composition (Column 2, lines 50-54). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made that the ratio recited in Claim 19 i.e. 2.5: 2.5: 5 would be inherent in the 2 to 20% recited in Bresser et al. and it would have been further obvious to the skilled practitioner apply the range of percentages taught by Bresser et al. to optimize precipitation and infusion based on cell type being assayed and desired results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

#### ***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992) as applied to claim 1 above, and further in view of Hames et al. (Nucleic Acid Hybridization: A practical approach, 1988, pages 193-194).

Regarding Claims 10-12, Bresser et al. teach the effective time period is 30 minutes and the effective temperature is 42°C (Column 10, lines 40-42). Bresser et al. do not teach the effective time period of one to four days and the effective temperature of room temperature or 0°C to 40°C. However, it was known in the art at the time the claimed invention was made that

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techniques for stabilizing cells are cell-type specific as taught by Hames et al. and depend upon cell membrane and type of nucleic acid being studied. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the method for Bresser et al. with the teaching of Hames et al. to obtain the claimed invention because one of ordinary skill in the art would have been motivated with a reasonable expectation of success to adjust the time and temperature for stabilizing the cells based on the teaching of Hames et al. for the expected benefit of optimizing stabilization.

9. Claims 21 & 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992) as applied to claim 17 above.

Regarding Claim 21, Bresser et al. disclose the composition wherein said first substance is a precipitating agent i.e. alcohol and said second substance is dimethyl sulfoxide (Column 2, lines 50-54 and Claim 1, lines 25-26). It was known to one of skill in the art at the time the claimed invention was made that methanol is a precipitating agent as taught by Bresser et al. (Column 7, line 40). Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Bresser et al. with the teaching of Bresser et al. to obtain the claimed invention because the skilled practitioner would have been motivated with a reasonable expectation of success to use methanol as the precipitating agent in the method of Bresser et al. based on cell type being assayed, available reagents and known precipitating properties.

Regarding Claim 23, Bresser et al. disclose the method wherein said first substance is ethanol and said second substance is dimethyl sulfoxide (Claim 2, lines 47-48).

10. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992) as applied to claim 20 above. Bresser et al.

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disclose the composition wherein said first substance is a precipitating agent i.e. alcohol and said second substance is dimethyl sulfoxide (Column 2, lines 50-54 and Claim 1, lines 25-26). It was known to one of skill in the art at the time the claimed invention was made that methanol is a precipitating agent as taught by Bresser et al. (Column 7, line 40). Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Bresser et al. with the teaching of Bresser et al. to obtain the claimed invention because the skilled practitioner would have been motivated with a reasonable expectation of success to use methanol as the precipitating agent in the method of Bresser et al. based on cell type being assayed, available reagents and known precipitating properties.

11. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992) as applied to claim 19 above. Bresser et al. disclose the method wherein the first substance is a precipitating agent and is comprised of a first alcohol i.e. polyethylene glycol and a second alcohol i.e. dithiothreitol (Hybridization Cocktail, Column 8, lines 65-67 and Column 9, lines 1-4). It was known to one of skill in the art at the time the claimed invention was made that methanol and ethanol are precipitating agents as taught by Bresser et al. (Column 7, lines 39-40). Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Bresser et al. with the teaching of Bresser et al. to obtain the claimed invention because the skilled practitioner would have been motivated with a reasonable expectation of success to use two alcohols having the same functions i.e. as precipitating agents, with the infusion agent in the method of Bresser et al. and to optimize their concentration ratio based on cell type being assayed and known precipitating properties.

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12. Claims 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bresser et al. (U.S. Patent No. 5,521,061, filed 17 July 1992) as applied to claim 13 above, and further in view of Hames et al. (Nucleic Acid Hybridization: A practical approach, 1988, pages 193-194).

Regarding Claims 28-30, Bresser et al. teach the effective time period is 30 minutes and the effective temperature is 42°C (Column 10, lines 40-42). Bresser et al. do not teach the effective time period of one to four days and the effective temperature of room temperature or 0°C to 40°C. However, it was known in the art at the time the claimed invention was made that techniques for stabilizing cells are cell-type specific as taught by Hames et al. and depend upon cell membrane and type of nucleic acid being studied. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the method for Bresser et al. with the teaching of Hames et al. to obtain the claimed invention because one of ordinary skill in the art would have been motivated with a reasonable expectation of success to adjust the time and temperature for stabilizing the cells based on the teaching of Hames et al. for the expected benefit of optimizing stabilization.

### ***Conclusion***

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8742 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.  
April 12, 2000

S. Forman

U.S. Patent and Trademark Office